Remarks

In the Office Action mailed November 14, 2008, the Examiner rejected specification for failure to comply with one or more of the requirements of 37 C.F.R. § 1.821 through 1.825 in relation to the nucleotide sequences. Applicants have amended the specification to add the sequence identifiers to the specification. By way of making these entries, Applicants submit that no new matter has been added.

35 U.S.C. § 102(b) as being anticipated by Butcher (1999)

In the Office Action mailed November 14, 2008, the Examiner rejected claims 21-26, 28, 30, and 32-34 under 35 U.S.C. § 102(b) as anticipated by the non-patent literature reference of David Butcher, *Microchemical Journal*, 62, 351-362 (1999), hereinafter referred to as Butcher.

The Applicants will first discuss claim 21, which is listed below, as amended, for the Examiner's convenience.

> 21. A device for fragmenting a peptide ion or protein ion substantially at one or more of the α-carbon--carbonyl carbon bonds present in the peptide ion or protein ion, the device comprising:
>
> a first component capable of forming the peptide ion or protein ion from a sample,
>
> a second component comprising a source of vacuum ultraviolet radiation adapted to deliver light at an energy sufficient to break at least one of the one or more α-carbon--carbonyl carbon bonds and produce one or more fragments of the peptide ion or protein ion, and
>
> a third component comprising a first mass analyzer, where the mass analyzer is operably connected to receive the one or more fragments of the peptide ion or protein ion.

Applicants point out that the elements within dependent claims 24 - 26 have been incorporated into claim 21, accordingly those claims are being canceled. One element of claim 21 is "a first component capable of forming the peptide ion or protein ion from a sample." Applicants respectfully submit that Butcher fails to teach or include at least this element of claim 21. Specifically, Butcher does not teach or include a first component capable of forming the peptide ion or protein ion from a sample. The Examiner has stated

that "a component capable of forming the peptide or protein ion from a sample" is shown on page 356, Fig. 1 of Butcher. However, Fig. 1 of Butcher illustrates that the sample is introduced into the chamber through a leak valve. One of ordinary skill in the art will appreciate that a leak valve is not capable of forming a peptide ion or protein ion from a sample. One of ordinary skill understands that leak valves are useful for introducing volatile molecules or gases into a device such as that shown by Butcher. In other words, the disclosure of Butcher provides no means for forming a peptide ion or protein ion from a sample. This is further supported by the Butcher's teaching that the single-photoionization method is useful for volatile compounds [see paragraph 5, page 357; "SPI is characterized as a soft ionization method for gas phase species."]. The Applicants further point out that Butcher's entire disclosure is a methodology for *ionizing* molecules with vacuum ultraviolet radiation. However, claim 21 is directed to a device for fragmenting a peptide ion or protein ion. Applicants submit that these purposes, and the devices capable of such purposes, are distinct. To clarify this further, independent claim 21 has been amended to include elements from the dependent claims so that this distinction is clearly set forth within claim 21. Specifically, an element of claim 21 is a component adapted to deliver vacuum ultraviolet to produce fragments of ions. This can be easily contrasted from the device of Butcher which creates ions from uncharged molecules. In fact, Butcher teaches against fragmenting, stating that vacuum ultraviolet is particularly suited at avoiding fragmentation, "[a]dvantages of the use of vacuum ultraviolet include...minimal ion fragmentation." [abstract, line 2-4] Each of the pending dependent claims includes each limitation of claim 21 and are patentable for at least the these reasons.

Applicants respectfully remind the Examiner of the obligations under 37 C.F.R. §1.104 (c) (2) which states,

> In rejecting claims for want of novelty or for obviousness, the examiner must cite the best references at his or her command. When a reference is complex or shows or describes inventions other than that claimed by the applicant, the particular part relied on must be designated as nearly as practicable. The pertinence of each reference, if not apparent, must be clearly explained and each rejected claim specified.

If the examiner continues to assert that Butcher anticipates claim 21, Applicants request that the particular part relied on be designated for each element. Furthermore, Applicants submit that anticipation based generally on "Figure 1, pg. 356" does not sufficiently make apparent the pertinence of this reference to claim 21. Therefore, a clear

explanation regarding this pertinence is requested. Each of the claims 21-24, 28, and 32-34 are patentable over Butcher and Applicants respectfully request withdrawal of these rejections.

35 U.S.C. § 102(b) as being anticipated by Muhlberger (2002)

The Examiner rejected claims 21-26, 28-29, 34 under 35 U.S.C. § 102(b) as anticipated by the non-patent literature reference of F. Muhlberger et al., *Analytical Chemistry*, 74, 3790-3801 (2002), hereinafter referred to as Muhlberger.

Applicants respectfully point out that one element of claim 21 is "a first component capable of forming the peptide ion or protein ion from a sample." The examiner has pointed to page 3794, Fig. 2 to recite the element of a component capable of forming the peptide or protein ion from a sample; however, the teaching of Muhlberger is completely devoid of any reference to a component capable of forming a peptide ion or protein ion from a sample. In fact, Muhlberger is completely devoid of any reference to a peptide or protein. Muhlberger is similar to Butcher in that it is directed to a method for using vacuum ultraviolet radiation for soft ionization of molecules. However, claim 21 is directed to a device for fragmenting a peptide ion or protein ion. Applicants again submit that these purposes are distinct. As with Butcher, Muhlberger teaches against fragmenting stating, "[o]ne feasible approach for this purpose is the use of mass spectrometry (MS) with a selective and soft (fragment-free) ionization technique , such as chemical ionization (CI) or photo ionization (PI). Single photon ionization (SPI) with vacuum ultraviolet (VUV) light is a particularly soft ionization technique..." [abstract, line 3-9].

As requested above, if the examiner continues to assert that Muhlberger anticipates claim 21, Applicants request that the particular part relied on be designated for each element. It is not clear to the Applicants how a reference, which is completely devoid of any mention of a peptide or protein, can be used by the examiner to reject a claim directed towards a device for fragmenting a peptide ion or protein ion. Therefore, a clear explanation regarding the pertinence of Muhlberger to claim 21 is requested. Each of the claims 21-24, 28-29, 34 are patentable over Muhlberger and Applicants respectfully request withdrawal of these rejections.

35 U.S.C. § 102(b) as being anticipated by Baldwin (2002)

The Examiner rejected claims 21, 23-26, 28-34 under 35 U.S.C. § 102(b) as anticipated by the non-patent literature reference of Michael A. Baldwin et al., *Analytical Chemistry*, 73, 1707-1720 (2001), hereinafter referred to as Baldwin.

One element of claim 21 is a second component comprising a source of vacuum ultraviolet radiation. The Examiner has pointed to page 1709, left column, second full paragraph, to allege that Baldwin includes a source of vacuum ultraviolet radiation; however, Applicants submit that the Examiner has failed to understand the content of the Baldwin reference. For the Examiner's convenience, the referred to section of Baldwin is included here:

> Laser pulses were generated externally via a nitrogen laser (Laser Science Inc., VSL-337ND) operating at 337.1 nm. The laser was directed to the target via a 200-μm fiber-optic cable, removing the necessity for careful laser alignment. The output of the fiber optic was transmitted through the vacuum housing via an optical lens, illuminating the sample with an elliptical image ~200 μm by ~500 μm (~0.1 mm^2 in area). The spot was elliptical in nature due to the angle of incidence of the laser onto the target. The laser power was software controlled via an attenuator located directly at the laser output. The typical laser fluence for the experiments described here was 50-150 mJ/cm^2.

The Baldwin reference is completely devoid of any inclusion or teaching of a vacuum ultraviolet radiation source, including this excerpt. The Examiner has correctly identified that Baldwin teaches using a laser which operates at 337.1 nm; however, this is not a vacuum ultraviolet radiation source. Specifically, this wavelength is not within the range of wavelengths that one of ordinary skill in the art would consider vacuum ultraviolet radiation. While the ultraviolet light disclosed in Baldwin does pass into a vacuum chamber, vacuum ultraviolet radiation is NOT ultraviolet light propagating within a vacuum. Rather, those of ordinary skill in the art recognize that the term vacuum ultraviolet is a term of art used to describe light with wavelengths from about 10 nm to about 200 nm; that is, the term vacuum ultraviolet describes a region of the electromagnetic spectrum. The fact that the applicants were using the term in this sense can be seen from paragraph [page 8, line 4] where the applicants state that "...they absorb rather strongly in the vacuum ultraviolet (vacuum ultraviolet) region of the spectrum..." While this range is not specifically described in the Applicants disclosure, Applicants submit that range is well known in the art. Illustrative of

that fact that the range is well-known in the art is that both Butcher and Muhlberger do describe vacuum ultraviolet radiation and are congruent with Applicants assertion that vacuum ultraviolet is a region of the electromagnetic spectrum. Within Butcher, the Applicants direct the Examiner's attention to page 354, under the heading "Theory" to page 357, first full paragraph. Within Muhlberger, the Applicants direct the Examiner's attention to page 3792, second column, through page 3795; Table 1 may be particularly useful.

Accordingly, the Examiner will appreciate that the ultraviolet light of Baldwin, at 337.1 nm, is clearly outside the range of light which is defined as vacuum ultraviolet light. Therefore, claim 21 and each claim that depends from claim 21are patentable over Baldwin and Applicants respectfully request withdrawal of these rejections.

35 U.S.C. § 103(a) as unpatentable over the combination of Baldwin, Muhlberger, and Butcher.

The Examiner rejected claims 21-34 under 35 U.S.C. 103(a) as being unpatentable over the combination of Baldwin, Muhlberger, and Butcher. As described above, the Applicants cancelled claims 24-26, incorporating those elements into claim 21.

The rejection of claims 21-34 is improper because Baldwin does not teach a device comprising a source of vacuum ultraviolet radiation as suggested by the examiner. The Supreme Court in KSR reaffirmed that certain principles govern the analysis of obviousness. One such principle is that the question of obviousness must be resolved on the basis of the factual inquiries enunciated by the Supreme Court in its landmark decision in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). The first of such factual inquiries is a determination of the scope and content of the prior art. In this regard, the rejections contained in the Office Action are flawed since they are predicated upon a misunderstanding of the teachings of Baldwin. As discussed above, an ultraviolet source radiating at 331.7 nm is not a vacuum ultraviolet light source. Also discussed above, the Examiner alleged that both Muhlberger and Butcher included or taught a first component capable of forming the peptide ion or protein ion from a sample; however, this allegation is not supported by either reference. Muhlberger is completely devoid of any mention of a protein or peptide and Butcher teaches that the single-photoionization method is useful only for volatile compounds [see paragraph 5, page 357; "SPI is characterized as a soft ionization method for gas phase species."].

Also described above, both Muhlberger and Butcher teach against fragmenting with the vacuum ultraviolet light sources. Rather, both teach a "soft" single-photoionization method. "Soft" single-photoionization is a way to generate ions from a molecular sample without fragmenting the molecular species. The device of claim 21 is "for fragmenting a peptide ion or protein ion." The purpose of the device of claim 21 is distinct from and in conflict with the purpose of the vacuum ultraviolet described by both Muhlberger and Butcher; their purpose being to avoid fragmentation. Furthermore, in both Muhlberger and Butcher, the vacuum ultraviolet was used to ionize (i.e. generate ions from a molecular species). Claim 21 is a device for *fragmenting* ions. Therefore, Muhlberger's and Butcher's vacuum ultraviolet source irradiates molecules to form ions and the vacuum ultraviolet interacts with non-ionic molecules. This is contrasted to claim 21 in which the vacuum ultraviolet is adapted to deliver light to ions.

Accordingly, in light of the fact that (i) the factual inquiry regarding each reference is fundamentally flawed and (ii) both Muhlberger and Butcher actually teach away from fragmenting, the Applicant submits that the subject combination does not render independent claim 21 obvious. Each of the dependent claims are patentable for at least these reasons. Accordingly, the Applicant respectfully requests that the rejection of claims 21-34 be withdrawn.

CONCLUSION

The foregoing remarks are believed to be fully responsive to the various rejections raised by the Examiner in the November 14, 2008 Office Action. Applicant believes that this application is in condition for allowance, and respectfully request passage of the application to issuance.

Respectfully submitted,

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